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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,431	01/30/2004	Daniel J. Thompson	25871	6428

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EXAMINER

ARNOLD, ERNST V

ART UNIT PAPER NUMBER

1616

DATE MAILED: 06/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	10/767,431		THOMPSON ET AL.	
	Examiner		Art Unit	
	Ernst V. Arnold		1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-27 is/are rejected.
- 7) ☒ Claim(s) 17 and 19 is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>7/30/2004</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

The Examiner acknowledges receipt of application number 10/767,431 filed on 01/30/2004. Claims 1-27 are pending in the application.

Applicant is advised that "polyglyceryl -3- oleate" should be written as --- polyglyceryl-3-oleate---. Applicant is advised to remove the period after nitrate in claim 19. Applicant is advised in claim 6 that "polyglyveryl" is spelled polyglyceryl.

Claim Objections

Claim 17 is objected to because of the following informalities: claim 17 recites the limitation "application". The Examiner suggests that Applicant amend the claim using the active word "applying". Appropriate correction is required.

Claim 19 is objected to because of the following informalities: claim 19 recites the limitation "administration". The Examiner suggests that Applicant amend the claim using the active word "administering". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-16, 19, 20, 21 and 24-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear to the Examiner

how a method for the treatment of an undiagnosable vulvovaginitis condition can comprise treating a condition caused by a species of *Candida*, which must have been diagnosed in order for it to be known. Otherwise how would one of ordinary skill in the art know that the condition was caused by a species of *Candida*? For purposes of examination, the Examiner will interpret the claims as it reads upon a candidiasis condition.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9 and 24-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Brown et al. (The Journal of Reproductive Medicine 1999, 44(11), 933-938) in view of Stedman's medical dictionary 24th edition 1982, page 334.

Brown et al. disclose the use of a single dose cream formulation of 2% butoconazole nitrate for vulvovaginal candidiasis (Page 933, title, objective, results). Stedman's medical dictionary defines cream as: a semisolid emulsion of either the oil-in-water or the water-in-oil type, ordinarily intended for topical use. Thus, the cream disclosed by Brown et al. is inherently a multiphase formulation. Brown et al. disclose that of the 150 known species of *Candida*, only nine are pathogenic in humans, which are *albicans*, *glabrata*, *tropicalis*, *pseudotropicalis*, *lusitaniae*, *crusei*, *rugosa*,

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parapsilosis and *guilliermondi* (Page 934, left column). The Examiner interprets this to mean that Brown et al. define candidiasis as being caused by any of these species of *Candida*. Brown et al. disclose that the patients administered the butoconazole cream with an applicator and that the cream was spread over vaginal mucosal surfaces (Page 935, Study Drugs and their assignment). Brown et al. disclose a cure rate of 92% using single dose butoconazole cream with a kill rate over 50% in 4 days (Page 936, Table 1 and page 937, Figure 1). Brown et al. disclose that the single application regimen, efficacy and safety support the use of butoconazole for the management of vulvovaginal candidiasis (Page 938, last paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Riley (US 5,266,329) in view of Brown et al. (The Journal of Reproductive Medicine 1999, 44(11), 933-938) and Garg et al. (Pharmaceutical Technology Drug Delivery 2001, 14-24) and Droegemueller et al. (Obstet Gynecol. 1984, 64(4), 530-4).

Applicant claims: A method for the local treatment of a vulvovaginal candidiasis condition diagnosable by a KOH smear test or other fungal speciation test, which comprises: treating said vulvovaginal candidiasis condition caused by a species of Candida selected from the group consisting of dubliniensis, tropicalis, glabrata, parapsilosis, krusei, and lusitaniae by applying to the vaginal tissue of a human a formulation comprising; about 35 to about 45% w/w sorbitol solution; about 3 to about 8% w/w propylene glycol; about 0.001 to about 1% w/w edetate disodium; about 5 to about 11% w/w mineral oil; about 0.5 to about 5% w/w polyglyceryl -3- oleate; about 0.5 to about 5% w/w glyceryl monoisostearate; about 0.001 to about 1% w/w microcrystalline wax; about 0.5 to about 2% w/w silicon dioxide; about 0.001 to about 1% w/w methylparaben; about 0.001 to about 1% w/w propylparaben; about 25 to about 45% w/w water; and about 0.5 to about 5% w/w butoconazole nitrate; and wherein the treatment is a single dose treatment.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Riley teaches systems and methods of preparation and use that release an antifungal agent such as an imidazole in a controlled manner in a vaginal cavity

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(Abstract). Riley teaches a composition of (in % wt/wt): 42.895 water; 39.978 sorbitol solution; 2.00 metronidazole; 0.05 EDTA disodium; 4.016 dimethicone; 4.016 mineral oil; 2.713 glyceryl isostearate; 2.713 polyglyceryl-4 oleate; 1.013 colloidal silicon dioxide; 0.452 microcrystalline wax; 0.127 methylparaben; and 0.027 propylparaben (Column 6, lines 18-30). Note the ratio of polyglyceryl-4 oleate to glyceryl isostearate is 1:1. Riley teaches methods of treating a vaginal fungal infection wherein the active antimicrobial agent is an imidazole agent (Claims 4 and 7).

The reference of Brown et al. is discussed in detail above and that discussion is hereby incorporated by reference. Brown et al. teach the use of a single dose cream formulation of 2% butoconazole nitrate for vulvovaginal candidiasis (Page 933, title, objective, results). Brown et al. teach that of the 150 known species of *Candida*, only nine are pathogenic in humans, which are *albicans*, *glabrata*, *tropicalis*, *pseudotropicalis*, *lusitaniae*, *crusei*, *rugosa*, *parapsilosis* and *guilliermondi* (Page 934, left column). Brown et al. teach that the patients administered the butoconazole cream with an applicator (Page 935, Study Drugs and their assignment). Brown et al. teach that the butoconazole cream would adhere to the vaginal mucosal surface for a prolonged period and that of the 29% of the patients that reported vaginal leakage only 1% of the patients treated found vaginal leakage unacceptable (Page 935, left column and page 938, left column). Brown et al. teach a cure rate of 92% using single dose butoconazole cream with a kill rate over 50% in 4 days (Page 936, Table 1 and page 937, Figure 1).

Garg et al. teach pharmaceutical excipients for vaginal formulations and list propylene glycol as a humectant; preservative; solvent or cosolvent in the formulations (Page 21).

Droegemueller et al. teach that one dose of 2 % butoconazole nitrate vaginal cream results in a maximum plasma level 24 hours after dosing (Abstract).

Chen et al. teach improved delivery of therapeutic agents, including anti-fungal agents, such as butoconazole, in a composition comprising polyglyceryl 2-4 oleate (Abstract; column 29, line 19 and claim 34, for example).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Riley does not expressly teach a method with about 3 to about 8% w/w propylene glycol in the composition.

Riley does not expressly teach a method with about 0.5 to about 5% w/w butoconazole nitrite in the composition.

Riley does not expressly teach a method comprising treating a vulvovaginal candidiasis condition with a composition comprising polyglyceryl-3-oleate.

Riley does not expressly teach a method wherein the treatment provides peak plasma levels of the butoconazole nitrate at about 6 to about 48 hours after administration and retains activity for at least 4 days.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add propylene glycol, as suggested by Garg et al., butoconazole, as suggested by Brown et al. and polyglyceryl-3-oleate, as suggested by Chen et al. to the composition of Riley and produce the instant invention. The instantly claimed limitations of a peak plasma level of administration of butoconazole nitrate at about 6 to about 48 hours after administration is taught by Droegemueller et al. Brown et al. demonstrate the effectiveness for at least 4 days.

One of ordinary skill in the art would have been motivated to do this because Riley suggests imidazole anti-fungals for use in the composition and Brown et al. demonstrate the effectiveness of butoconazole in single dose. The addition of propylene glycol is known by one of ordinary skill the art as an excipients for vaginal formulations as taught by Garg et al. Chen et al. establish the equivalency of using polyglyceryl-2-oleate, polyglyceryl-3-oleate or polyglyceryl-4-oleate in anti-fungal drug delivery formulations. The adjustment of particular working conditions (e.g., determining the amount of propylene glycol or other ingredients to be used in the formulation and the determination of the type of species of *Candida*) is deemed merely a matter of judicious selection and routine optimization, which is well within the purview of one of ordinary skill in the art.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed

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invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

No claims are allowed.

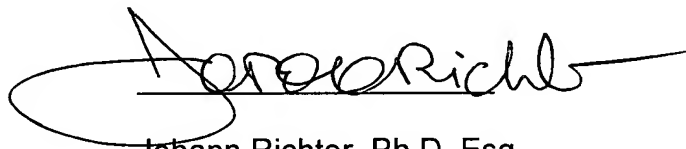
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ernst Arnold
Patent Examiner
Technology Center 1600
Art Unit 1616
May 02, 2006

A handwritten signature in black ink, appearing to read "Johann Richter", written over a horizontal line. The signature is stylized with a large initial "J" and a long horizontal stroke at the end.

Johann Richter, Ph.D. Esq.
Supervisory Patent Examiner
Technology Center 1600